

We claim:

1. A targeting construct comprising:
  - (a) a first polynucleotide sequence homologous to a serine protease gene;
  - (b) a second polynucleotide sequence homologous to the serine protease gene;
  - 5 and
  - (c) a selectable marker.
2. The serine protease targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
  - 10 (a) providing a first polynucleotide sequence homologous to a serine protease gene;
  - (b) providing a second polynucleotide sequence homologous to the serine protease ;
  - (c) providing a selectable marker; and
  - 15 (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the serine protease targeting construct.
4. A method of producing a targeting construct, the method comprising:
  - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a serine protease gene and a second sequence homologous to a serine protease gene;
  - 20 (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
5. A cell comprising a disruption in a serine protease gene.
6. The cell of claim 5, wherein the cell is a murine cell.
- 25 7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a serine protease gene.
9. A cell derived from the non-human transgenic animal of claim 8.
10. A method of producing a transgenic mouse comprising a disruption in a serine protease gene, the method comprising:
  - 30 (a) introducing the targeting construct of claim 1 into a cell;
  - (b) introducing the cell into a blastocyst;

- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a serine protease,  
5 the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a serine protease gene;
- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the expression of serine protease in the non-human  
10 transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a serine protease,  
the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a serine protease gene;
- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the function of the disrupted serine protease gene in the  
15 non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of serine protease,  
the method comprising:

- (a) providing a cell comprising a disruption in a serine protease gene;
- (b) contacting the cell with an agent; and
- (c) determining whether expression of the serine protease is modulated.

14. A method of identifying an agent that modulates the function of a serine protease  
gene, the method comprising:

- (a) providing a cell comprising a disruption in a serine protease gene;
- (b) contacting the cell with an agent; and
- (c) determining whether the function of the serine protease gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-  
human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.